Remarks

Claims 1 and 2 remain pending. Claim 3 was cancelled in the Amendment filed October 6, 2003 in order to facilitate prosecution. Applicants thank the Office for acknowledging and entering the amendments made in the Response and Amendment under 37 C.F.R. § 1.196(b)(1) to the Decision of the Board of Patent Appeals and Interferences, filed October 6, 2003.

1. The Objection Under 35 U.S.C. § 132

The specification has been objected to under 35 U.S.C. § 132 for the Amendment filed on September 13, 2000, because the amendment to the specification allegedly contained new matter. Office Action at page 2. Applicants respectfully disagree.

The Office Action alleges that the added material which is not supported by the original disclosure is "the material inserted into the original specification at page 18, line 18, relating to a clone LIB3049-003-Q1-E1-H7, later designated ATCC No. PTA-2416, and the statement that SEQ ID NO: 1 is the sequence of the deposited clone." Office Action at page 2. According to the Office, the support for this material cited in the specification does not show "any connection made between the source of SEQ ID NO: 1 and the LIB3049 library, i.e. it neither indicates that a clone of the library was used to determine SEQ ID NO: 1, nor that any clone of the library comprised a nucleic acid whose sequence is SEQ ID NO: 1." *Id.* at pages 2-3. Applicants respectfully disagree with these assertions.

Applicants have previously submitted a Declaration Under 37 C.F.R. § 1.132, executed by Thomas J. La Rosa, dated September 11, 2000 ("First La Rosa Declaration"). Applicants have also previously submitted a Declaration Under 37 C.F.R. § 1.132, executed by Roger C. Wiegand, Ph.D., dated August 17, 2000 ("Wiegand Decl."). Applicants respectfully submit that both of these previously-filed declarations support the assertion that the amendment made to the specification filed on September 13, 2000 did not contain new matter. However, in order to

provide additional clarification, Applicants have filed herewith a second Declaration Under 37 C.F.R. § 1.137 by Thomas J. La Rosa, dated May 20, 2004 ("Second La Rosa Decl.").

The Second La Rosa declaration evidences that the amendment to the specification filed on September 13, 2000 is not new matter. First, the Second La Rosa Declaration reiterates that the library designated LIB3049 is the source of the soybean clone designated LIB3049-003-Q1-E1-H7. Second, the Second La Rosa Declaration reiterates that the insert of clone LIB3049-003-Q1-E1-H7 contains a nucleic acid molecule comprising SEQ ID No. 1, identified in the 09/206,040 specification. Moreover, the Second La Rosa Declaration acknowledges that the 09/206,040 specification sets forth that a cDNA insert from LIB3049 is ligated and inserted into a pSport vector and that the LIB3049-003-Q1-E1-H7 clone contains, in part, the nucleotide sequence of SEQ ID No. 1. *See* Second La Rosa Decl. at ¶s 4, 5 and 7.

Therefore, all of the stated grounds for the objection to the amendment filed on September 13, 2000 have been overcome. *See* Office Action at page 3. Thus, Applicants respectfully request withdrawal of the objection to the specification under 35 U.S.C. § 132.

2. The Claimed Nucleic Acid Molecules Meet the Utility Requirement of 35 U.S.C. § 101

The Office has rejected claims 1 and 2 under 35 U.S.C. § 101 because the claimed invention is allegedly "not supported by either a specific and substantial asserted utility or a well established utility". Office Action at page 4. The Office Action, in part, reiterates the statements made in the Decision of the Board of Patent Appeals and Interferences mailed August 20, 2003 (Paper No. 26) ("Board Decision"). *See* Office Action at pages 4-19. In addition, the Office Action acknowledges each of the utilities disclosed in Applicants' specification for the claimed nucleic acid molecules, but maintains that

> . . .the disclosed utilities are *non-specific* utilities, since any of the general disclosed utilities would apply equally to any uncharacterized nucleic acid molecule from soybean in particular, or plant or other organisms in general. Moreover, since practice of these utilities would first require research on the disclosed EST itself, *i.e.*, there is no apparent *immediate* benefit to the public,

> the disclosed utilities are not substantial. The only readily apparent *immediate* use for the disclosed EST is as an object of further scientific inquiry aimed at characterization of the EST itself in terms of identity of corresponding sequence polymorphisms (if any), map location, sequence and function of the corresponding mRNA and polypeptide, tissue distribution of the corresponding mRNA and polypeptide, *etc.* These *immediate* uses are merely searches for a specific and substantial statutory utility for the claimed invention that fail to meet the statutory utility requirement.

Office Action at pages 20-21, *citing Brenner v. Manson*, 383 U.S. 519, 534-35, 148 U.S.P.Q. 689, 696 (1966) (emphasis in original).

This analysis misstates the nature of the asserted uses, ignores disclosed utilities, and misapplies the doctrine of "practical utility" developed by the courts after *Brenner v. Manson*. It is well-established law that "when a properly claimed invention meets at least one stated objective, utility under section 101 is clearly shown." *Raytheon Co. v. Roper Corp.*, 724 F.2d 951, 958, 220 U.S.P.Q. 592, 598 (Fed. Cir. 1983). The "threshold for utility is not high: An invention is 'useful' under section 101 if it is capable of providing some identifiable benefit." *Juicy Whip, Inc. v. Orange Bang, Inc.*, 185 F.3d 1364, 1366, 51 U.S.P.Q.2d 1700, 1702 (Fed. Cir. 1999), *citing Brenner v. Manson*, 383 U.S. 519, 534 (1966). Furthermore, an invention need only provide <u>one</u> identifiable benefit to satisfy 35 U.S.C. § 101. *See Raytheon Co. v. Roper Corp.*, 724 F.2d 951, 958, 220 U.S.P.Q. 592, 598 (Fed. Cir. 1983) ("when a properly claimed invention meets at least one stated objective, utility under section 101 is clearly shown"). Applicants respectfully traverse the rejection, because the claimed nucleic acid molecules are supported by specific, well-established "real world" utilities as described in the specification and as proven by experimentation. Although Applicants only need to establish a single utility to satisfy 35 U.S.C. § 101, all of the issues raised by the Office are addressed herein.

The courts have expressed a test for utility that hinges on whether an invention provides an "identifiable benefit." *Juicy Whip, Inc. v. Orange Bang, Inc.*, 185 F.3d 1364, 1366, 51 U.S.P.Q.2d 1700, 1702 (Fed. Cir. 1999), *citing Brenner v. Manson*, 383 U.S. 519, 534 (1966). For analytical purposes, the requirement for an "identifiable benefit" may be broken into two

prongs: (1) the invention must have a specific, *i.e.*, not vague or unknown benefit, *In re Brana*, 51 F.3d 1560, 1565, 34 U.S.P.Q.2d 1436, 1440 (Fed. Cir. 1995); and (2) the invention must provide a real world, *i.e.*, practical or "substantial" benefit. *Fujikawa v. Wattanasin*, 93 F.3d 1559, 1563, 39 U.S.P.Q.2d 1895, 1899 (Fed. Cir. 1996). A corollary to this test for utility is that the invention must not be "totally incapable of achieving a useful result," *i.e.*, the utility must not be incredible or unbelievable. *Brooktree Corp. v. Advanced Micro Devices, Inc.*, 977 F.2d 1555, 1571, 24 U.S.P.Q.2d 1401, 1412 (Fed. Cir. 1992).

Applicants have not only asserted, but have substantiated their assertions with experimental proof that the claimed nucleic acid molecules provide identifiable benefits, *i.e.*, use to identify the presence or absence of a polymorphism, and use as a hybridization probe for expression profiling. Either of these utilities alone is enough to satisfy Section 101. The Office continues to ignore Applicants' legally sufficient and uncontested assertions of utility and instead imposes an improper test for utility unsubstantiated by law. This it may not do. Because Applicants need only establish a single utility to satisfy 35 U.S.C. § 101, and they have done so in the present case, the premise of the rejection under Section 101 is incorrect, and the rejection should be reversed.[1]

A. The Claimed Nucleic Acid Molecules Provide a Specific Benefit, *i.e.*, They have Specific Utility

Contrary to the Office's assertion that "the disclosed utilities are *non-specific* utilities", the Office has acknowledged several specific utilities for the claimed nucleic acid molecules that

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[1] Despite the Office's acknowledgement that the claimed invention is operable for at least one objective disclosed in the specification, *i.e.*, "the nucleic acid molecules do detect polymorphisms," Advisory Action mailed November 22, 2000 ("Advisory Action"), at page 12, the utility rejection continues to be maintained. No legal basis has been provided in support of maintaining a utility rejection of an invention that meets the statutory criteria for utility. 35 U.S.C. § 131 states that "if on such examination [by the Patent Office] it appears that the applicant is entitled to a patent under the law, the Director shall issue a patent therefor." Applicants have shown that their claimed invention satisfies the statutory criteria of Section 101 as interpreted by the courts. This proof cannot be ignored.

have been disclosed in the present specification.[2] *See, e.g.,* Office Action at pages 19-20, specification at page 24, line 4 through page 44, line 21; page 63, line 12, through page 65, line 25. Moreover, Applicants have asserted specific utilities for the claimed nucleic acid molecules in the specification, and have proven by experimentation that the claimed nucleic acid molecules work for at least two of the asserted utilities: use to identify the presence or absence of a polymorphism and use as a hybridization probe for expression profiling. The law requires nothing more. *See Raytheon Co. v. Roper Corp.*, 724 F.2d 951, 958, 220 U.S.P.Q. 592, 598 (Fed. Cir. 1983) ("when a properly claimed invention meets at least one stated objective, utility under section 101 is clearly shown").

According to the Office Action, the disclosed utilities are not specific because they allegedly "would apply equally to any uncharacterized nucleic acid molecule from soybean in particular, or plants or other organisms in general." Office Action at page 20. That position is wrong as a matter of law – there is no requirement of exclusive utility in the patent law. *See Carl Zeiss Stiftung v. Renishaw PLC*, 945 F.2d 1173, 1180, 20 U.S.P.Q.2d 1094, 1100 (Fed. Cir. 1991) ("An invention need not be the best or the only way to accomplish a certain result..."). Applicants have not only asserted that the claimed nucleic acid molecules work for the disclosed utilities, but have provided experimental proof that supports their position. In contrast, the Office has not provided any evidence suggesting that the claimed nucleic acid molecules would not work for the disclosed utilities.

Nor is it true that the claimed nucleic acid molecules are "uncharacterized". Office Action at page 15. Applicants have disclosed a number of characteristics of the claimed nucleic acid molecules, including the identity of specific plant tissue expressing the corresponding

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[2] For example, the Office Action lists several utilities disclosed in the present specification for the claimed nucleic acid molecules: (1) use of the EST as a probe to detect and identify sequence polymorphisms, which can be used as molecular markers; (2) use of the EST as a probe for detecting a physical map location (*e.g.*, as a marker in *in situ* hybridization); (3) use of the EST as a probe or source of primers; (4) use of the EST as an antisense inhibitor; and (5) use of the EST to identify or isolate proteins that bind to the EST sequence. *See* Office Action at pages 19-20.

mRNA, *i.e.*, young seed pods (5 to 15 days after flowering),[3] the origin of the clone from which SEQ ID No. 1 was sequenced, *i.e.*, *Glycine max* soybean cultivar Asgrow 3244, and the clone from which SEQ ID No. 1 was sequenced, *i.e.*, the clone designated "LIB3049-003-Q1-E1-H7." Specification at page 67, lines 11-12, page 24, line 4-5; Wiegand Decl. at ¶ 4; Sequence Listing at page 1. The Office ignores this disclosed information and continues to ignore the specific utilities disclosed by Applicants for the claimed nucleic acid molecules.

Additionally, Applicants have proven that the nucleotide sequence alone is all that is necessary to use the claimed nucleic acid molecules for the disclosed utilities, *e.g.*, to detect the presence or absence of polymorphisms. *See* Wiegand Decl. at ¶s 22-23. The corresponding mRNA and polypeptide sequence need not be characterized. It is irrelevant whether the corresponding mRNA or polypeptide themselves have utility because Applicants are not relying on utility of the mRNA or polypeptide to establish utility of the claimed nucleic acid molecules.

In any event, it cannot be said that the disclosed utilities are not specific or that the claimed nucleic acid molecules are not characterized. One of the disclosed utilities for the claimed nucleic acids is the ability to identify the presence or absence of a polymorphism. Specification at page 28, line 3 through page 35, line 3. The Office has never provided any evidence suggesting that the claimed nucleic acid molecules would not work for this utility. As the Wiegand Declaration demonstrates, the claimed nucleic acid molecule has been used to identify the presence of polymorphisms in a population of soybean plants. Wiegand Decl. at ¶s 22-23. This statement has been further confirmed in the declaration executed by Vergel Concibido on June 28, 2004, submitted herewith, ("Concibido Decl.") at ¶ 4. Because the

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[3] The Office asserts that "young seed pods are not tissue, although they comprise tissues" and that the specification "does not disclose which specific tissue(s) contained in the young seed pods expressed the mRNA" and therefore that the claimed nucleic acid molecules have no utility. Advisory Action at pages 10-12. This distinction has no bearing on the utility of the claimed nucleic acid molecules. Whether or not young seed pods are "tissue" is irrelevant. One skilled in the art would know that because the claimed nucleic acid molecules were isolated from young seed pods, they will provide an appropriate starting point for isolating a promoter that is active in young seed pods. Utility of such a promoter is discussed in Section 2.A.(3), *infra*.

claimed nucleic acid molecules work for the disclosed utilities, there is clearly a connection (correspondence) between the disclosed utilities and the claimed invention.

(1) Use of the Claimed Nucleic Acid Molecules

The Office Action argues that the disclosed utilities are directed to use of the claimed nucleic acid molecules as tools of scientific inquiry, and that such utilities lack legal significance. Office Action at page 21. This is wrong as a matter of law. The fact that, for example, a new and nonobvious microscope or screening assay can be used for learning about products or processes does not lessen the fact that such "tools" have legal utility. "Many research tools such as gas chromatographs, screening assays, and nucleotide sequencing techniques have clear, specific and unquestionable utility (*e.g.*, they are useful in analyzing compounds)." MPEP § 2107 at page 2100-33.

One legal utility of a microscope is its use to look at the structure of biological tissues placed under the microscope (electron microscopes can, of course, be utilized to look at intracellular structures). Many of the disclosed utilities in this case are directly analogous to the utilities of a microscope, *i.e.*, the claimed nucleic acid molecules may be used to locate and measure nucleic acid molecules within a sample, cell, or organism. The Office Action denigrates this utility by asserting that the "[t]hese *immediate* uses are merely searches for a specific and substantial statutory utility for the claimed invention. . ." Office Action at page 21 (emphasis in original). This assertion is untrue. The claimed nucleic acid molecules may be used to locate and measure nucleic acid molecules such as mRNA or chromosomal DNA that hybridize to SEQ ID No. 1 or its complement.

The specification also discloses additional utilities for the claimed nucleic acid molecules, including introduction of the claimed nucleic acid molecules into a plant or plant cell (either as sense or antisense inhibitors), which can then be used to screen for compounds such as a herbicide. Specification at page 64, line 19 through page 65, line 22. For example, a

compound can be provided to both an antisense plant and a control plant (no antisense) and the effect of the compound on the plant can be monitored. Such a screen is analogous to a cell-based assay, which has a legally sufficient utility.[4] Thus, the use in such a screen of a plant or plant cell having an introduced claimed nucleic acid molecule is a legally sufficient utility. Other utilities disclosed in the specification include use of the claimed nucleic acid molecules to measure the level of mRNA in a sample,[5] and use as molecular markers.[6]

(2) Use of the Claimed Nucleic Acid Molecules to identify the Presence or Absence of a Polymorphism

One of the utilities disclosed in the specification that has been addressed throughout prosecution of the application is use of the claimed nucleic acid molecules to identify the presence or absence of a polymorphism. Specification at page 28, line 3 through page 35, line 3. While there is no question that the claimed nucleic acid molecules will detect a polymorphism in a population of soybean plants, and this use has been substantiated by Applicants in repeated declarations as well as in the specification, the Office continues to collaterally attack the utility of this use. While the Office may argue that it has not "sidestepped the issue" in its repeated utility rejections (Office Action at page 36), the fact remains that Applicants have proven the claimed

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[4] *See, e.g.*, MPEP § 2107 at page 2100-33.

[5] It is standard practice to screen populations of nucleic acids with EST sequences, often attached to a microarray, without characterizing each and every target mRNA. Knowing that the gene corresponding to the claimed nucleic acid molecules is expressed under certain conditions or in certain tissues or at certain levels is in itself useful. *See* Wiegand Decl. at ¶ 14. For example, such information is useful to detect expression changes in traits of interest, *e.g.*, drought stress. Contrary to the Office's assertions, this is a use of the claimed nucleic acid molecules in a "real world" context. Office Action at page 21.

[6] One can use the claimed nucleic acid molecules to determine location of a corresponding DNA sequence on a physical map or genetic map location without knowing anything beyond the claimed sequence. *See* Wiegand Decl. at ¶ 12. The use of molecular markers is a practical activity in the development of nutritionally enhanced or agriculturally enhanced crops. Such markers are useful in, for example, genetic mapping or linkage analysis, marker-assisted breeding, physical genome mapping, transgenic crop production, crop monitoring diagnostics, and gene identification and isolation. As more markers are identified, genetic maps will become more detailed and it will be easier for plant breeders to breed for particular traits. *See* Applicants' Response filed August 22, 2000 ("Applicants' Second Response") at pages 11-12 and accompanying documents.

nucleic acid molecules may be used and, in fact, have been used to detect a polymorphism in a population of soybean plants. *See* Wiegand Decl. at ¶s 22-23; Concibido Decl. at ¶ 4. This utility alone is enough to satisfy the requirements of section 101.

The Office has made several suggestions for why the use of the claimed nucleic acid molecules does not support a finding of substantial utility. First, the Final Office Action mailed March 22, 2000 ("Final Action"), suggests that without the prior identification of a polymorphism, such use is legally insufficient "use testing." Final Action at pages 9-10. Second, the Advisory Action mailed November 22, 2000 ("Advisory Action"), suggests that identification of the presence or absence of a polymorphism, like a biological assay, has no utility "[i]f such an assay would only identify compounds that have no utility". Advisory Action at page 11. Third, the Office asserts that the work done by Dr. Wiegand allegedly "fails to support the existence of a polymorphism, as the term is defined in the specification". Office Action at page 35. Fourth, the Office apparently struggles with the meaning of a "true enough copy of SEQ ID NO: 1" as described by Dr. Wiegand and as used in his experiments. *Id.* at pages 14-15. Finally, the Office and the Board of Patent Appeals and Interferences ("Board") suggest that even if a polymorphism were detected, such a use is at the lowest end of some alleged "utility spectrum" created by the Office. *Id.* at pages 11-12, 31. All of these suggestions are wrong and fail to address that the claimed nucleic acid molecules have been used to detect a polymorphism.[7]

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[7] The Office "has the initial burden of challenging a presumptively correct assertion of utility in the disclosure." *In re Brana*, 51 F.3d 1560, 1567, 34 U.S.P.Q.2d 1436, 1441 (Fed. Cir. 1995). The utilities asserted in the specification must be accepted as factually sound unless the Patent Office cites information that undermines the credibility of the assertion. *Id.* The Examiner "must do more than merely question – [he] must set forth factual reasons which would lead one skilled in the art to question the objective truth of the statement of operability." *In re Gaubert*, 524 F.2d 1222, 1225-26, 187 U.S.P.Q. 664, 666 (C.C.P.A. 1975) (emphasis in original); MPEP § 2107.01 ("Office personnel are reminded that they must treat as true a statement of fact made by an applicant in relation to an asserted utility, unless countervailing evidence can be provided that shows one of ordinary skill in the art would have legitimate basis to doubt the credibility of such a statement.") Here the Office has not even attempted to meet this burden.

(a) Identification of a Polymorphism Using the Claimed Nucleic Acid Molecules is Not "Use Testing"

The Final Action suggests that without the prior identification of a polymorphism, such use is legally insufficient "use testing." Final Action at pages 9-10. However, the Final Action provides no support (legal or factual) for the proposition that before detection of polymorphisms can be recognized as a legal utility, actual polymorphisms must be shown to exist. This proposition suggests that a gas chromatograph is not useful for detection of chemical compounds until actual chemical compounds are proven to exist. Moreover, use of the claimed nucleic acid molecules to screen for polymorphisms is not "use testing" because it determines information about the plant and its genetic traits, not additional information about the claimed nucleic acid sequence.

The Advisory Action confuses use of the claimed nucleic acid molecules with "use testing." *See* Advisory Action at pages 11-12. The Final Action challenged the credibility of the use to identify the presence or absence of a polymorphism. Final Action at page 10. Applicants, while maintaining that the Office's challenge did not raise a proper *prima facie* case of non-utility, presented experimental evidence demonstrating that the claimed nucleic acid molecules are operable, *i.e.*, that they work successfully to identify the presence or absence of a polymorphism. Wiegand Decl. at ¶s 22-23; Applicants' Response dated August 22, 2000 at page 10. The Advisory Action then attempted to wave *In re Kirk* like a magic wand and convert this proof of operability into "use testing."[8] Advisory Action at pages 11-12. This cannot be done. The facts of *Kirk* are not similar to the present application, and *Kirk*'s condemnation of applications that fail to disclose any use for a claimed invention is not applicable to the present

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[8] The Advisory Action also asserts that the experiments performed by Dr. Wiegand were "necessary before one could begin to take the next step in determining how to exploit this characteristic of the claimed invention for a practical utility." Advisory Action at page 12. This is not true. The experiments themselves demonstrate a practical utility for the claimed nucleic acid molecules. The Advisory Action misses the "simple, incontrovertible fact" that the use of the claimed nucleic acid molecules to identify the presence or absence of polymorphisms is a use of the claimed nucleic acid molecules, not a preparatory step for another use.

application, which discloses multiple uses for the claimed nucleic acid molecules. *E.g.*, specification at page 28, line 3 through page 35, line 3 (identifying the presence or absence of polymorphisms), page 38, line 23 through page 41, line 18 (detecting the expression level/pattern of a protein or mRNA), etc. *Cf. In re Kirk,* 376 F.2d 936, 941 ("[i]t is what the compounds are disclosed to do that is determinative...") (emphasis added).

Use of the claimed nucleic acid molecules to detect the presence or absence of polymorphisms is no more legally insufficient than using a gas chromatograph to analyze the chemical composition of a gas – such use determines information about the gas, not the gas chromatograph. Even if the gas chromatograph detects the absence of a particular chemical element in the gas, that finding does not obviate the utility of the gas chromatograph itself. Information has been obtained about the gas.[9] Likewise, the claimed nucleic acid molecules have utility even if the absence of a particular polymorphism is detected. Indeed, the absence of a polymorphism usefully demonstrates that the two (or more) populations being compared share a common genetic heritage.

(b) Identifying a Polymorphism is a Substantial Use for the Claimed Nucleic Acid Molecules, Regardless of the Underlying Utility of the Polymorphism Detected

The Advisory Action argues that a screening assay, such as a cell-based screening assay "would only meet the utility requirement if certain conditions were met.... [including that] the specification would have to teach some practical utility for at least one ligand identified by the assay, e.g. use as a drug." Advisory Action at pages 8-9. This argument implies that a diagnostic test such as an ELISA has no patentable utility because it does not identify useful ligands. This

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[9] For example, gas sampled from crude oil may be analyzed by gas chromatography for the presence or absence of chlorine, which is toxic to catalysts used in gasoline refining even in very low concentrations. The absence of a peak at the molecular weight of chlorine indicates the absence of chlorine in the sample being tested, thereby providing useful information (no chlorine is present, therefore the catalyst will not be destroyed) to the refinery manager. *See, e.g.*, U.S. Patent No. 6,133,740 entitled "Chlorine Specific Gas Chromatographic Detector."

position is unsupportable. Furthermore, contrary to the Advisory Action's assertions, *Brenner v. Manson* does not hold that a screening assay does not meet the utility requirement. *Brenner* holds that a process which has no known use (or a process which has the sole known use of producing a compound which has no known use) is not patentable. *Brenner v. Manson*, 383 U.S. 519, 534-35, 148 U.S.P.Q. 689, 693-94 (1966). The utility of a screening assay such as a diagnostic assay is known, *i.e.*, use as a diagnostic tool.[10] Therefore, it is not prohibited from patentability by *Brenner*. Likewise, the utility of identifying the presence or absence of a polymorphism is known, *i.e.*, it demonstrates whether two (or more) organisms being compared do or do not share a common genetic heritage.

In any event, these arguments are beside the point because the claimed nucleic acid molecules did identify a polymorphism. The Declaration of Dr. Wiegand reports that a nucleic acid molecule having the sequence of SEQ ID No. 1 detects polymorphisms in soybean chromosomal DNA from the soy varieties *Glycine max* and *Glycine soja*. Wiegand Decl. at ¶s 22-23. The Wiegand Declaration also confirms that nucleic acid molecules capable of detecting polymorphisms are useful in plant breeding. *Id.* at ¶s 20, 23. The Advisory Action asserts, without support, that the Wiegand Declaration does not substantiate the disclosed utility of detecting polymorphisms because the specification defines polymorphisms as intraspecies variations and *Glycine max* and *Glycine soja* are "two different species of *Glycine*." Advisory Action at page 13. To the contrary, *Glycine max* and *Glycine soja* can be interbred to produce fertile offspring.[11] Moreover, as the Concibido Declaration makes clear, a person of ordinary skill in the art, reading the present disclosure, would recognize that "the claimed nucleic acid

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[10] In other words, the screening assay's utility arises from its ability to tell the practitioner if a blood or body fluid sample is infected with a disease organism, or not. *E.g.*, U.S. Patent Nos. 6,153,411 (issued November 28, 2000); 6,140,055 (issued October 31, 2000); and 6,120,776 (issued September 19, 2000).

[11] A species, by definition, is a group of organisms that are "able to interbreed and produce fertile offspring." Norah Rudin, *Dictionary of Modern Biology* 346 (1997); *Oxford Dictionary of Biochemistry and Molecular Biology* 610 (A. D. Smith *et al.*, eds., 1997).

sequence could encompass the detection of polymorphisms in species that interbred such as *Glycine max* and *Glycine soja.*" Concibido Decl. at ¶ 3. Regardless of the Office's assertions, however, the ability of the claimed nucleic acid molecules to detect to presence or absence of a polymorphism has been confirmed by the tests performed by Dr. Wiegand, and supports this assertion of utility for the claimed invention. *See* Wiegand Decl. at ¶s 22-23; Concibido Decl. at ¶ 4.

(c) The Claimed Nucleic Acid Molecules Detect Polymorphisms Within Species

While the Office acknowledges that the tests performed by Dr. Wiegand detected the presence of a polymorphism between *Glycine soja* and *Glycine max*, the Office argues that this does not prove utility of the claimed nucleic acid molecules because these are allegedly two different species and therefore this utility is not one described in the specification. In particular, the Office Action states:

> With respect to the showing in the Wiegand Declaration, Wiegand used a probe purported to be a "true copy" of SEQ ID NO: 1 to detect genomic DNA isolated from each of two species of the genus *Glycine*, *G. soja* and *G. max* (from which the EST of SEQ ID NO:1 was isolated). Wiegand determined that the probe detected restriction endonuclease fragments of different sizes between the two species (¶ 20-23), but does not report that any such variation was found between individuals of *G. max* (¶ 17-18). The latter results fails [sic] to support the existence of a polymorphism, as the term is defined in the specification, and thus any use requiring detection of polymorphisms. The former result is not relevant to the issue at hand, since genetic variation in nucleotide sequences between two different species of plant is not "polymorphism" [sic] as defined in the specification.

Office Action at pages 34-35. Setting aside the fact that the Office has never presented any proof that one of ordinary skill in the art would doubt the asserted utility of the claimed nucleic acid molecules to detect the presence or absence of a polymorphism (and thus had failed to carry its burden), the Office now attempts to turn the declaration of Dr. Wiegand on its head in support of

the assertion that the claimed nucleic acid molecules would not detect a polymorphism. This is absurd.

First, while the specification does state that a polymorphism "is a variation or difference in the sequence of the gene or its flanking regions that arises in some of the members of a species", there is nothing in the specification that would limit the definition of "species" as the Office would like. Specification at page 28. For example, as defined above, a species, by definition, is a group of organisms that are "able to interbreed and produce fertile offspring."[12] Second, as stated above, those of ordinary skill in the art would recognize the ability of *G. soja* and *G. max* to interbreed and produce fertile offspring. *See* Concibido Decl. at ¶ 3. Finally, regardless of the definition of species at hand, the fact is the claimed nucleic acid molecules did detect a polymorphism and this supports, rather than contradicts, this assertion of utility. The Office may attempt to discount this evidence, but it may not ignore it.

In addition to Applicants' repeated arguments, the Second La Rosa Declaration and the Concibido Declaration also support the assertion that the claimed nucleic acid molecules will, in fact, detect the presence or absence of polymorphisms between *Glycine max* varieties. Second La Rosa Decl. at ¶ 8, Concibido Decl. at ¶ 4. Although Applicants contend that the Office has repeatedly failed to present evidence that one of ordinary skill in the art would doubt the utility of the claimed nucleic acid molecules to detect the presence or absence of a polymorphism, and thus has not met the burden to sustain a utility rejection, the accompanying evidence by those of ordinary skill in the art cannot be disregarded.

(d) Evidence Based on a "True Enough Copy" of SEQ ID NO: 1 is Relevant to the Question of the Utility of SEQ ID NO: 1

In addition to ignoring evidence that the claimed nucleic acid molecules did actually detect a polymorphism in a population of soybean plants, the Office further attempts to discount

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[12] *See* footnote 11, *supra.*

the experiments of Dr. Wiegand by asserting that somehow they did not consider an exact copy of SEQ ID No: 1. The Board stated

> Nor does Dr. Wiegand's declaration assist appellants in this portion of their position on appeal. Dr. Wiegand discusses the use of EST's [sic] to generate probes in paragraphs 14-17 of his declaration. However, that work is based upon a synthetic probe stated to be a "true enough copy of SEQ ID No: 1." It is not apparent why evidence based upon a "true enough copy" of SEQ ID No: 1 is relevant in this appeal.

Board Decision at page 26; Office Action at pages 14-15.

It appears that the Office is confused on the issue of whether the probe used by Dr. Wiegand contained the nucleotides of SEQ ID No. 1. Although the Declaration of Dr. Wiegand explains to one of ordinary skill in the art of how the sequence of the probe used by Dr. Wiegand was determined, the Second La Rosa Declaration, which explains that the probe used by Dr. Wiegand in fact included the nucleotides of SEQ ID No: 1. *See* Second La Rosa Decl. at ¶ 7. Thus, there is no support for the assertion that the work performed by Dr. Wiegand would not be relevant to support the utility of a nucleic acid molecule comprising SEQ ID No. 1.

(e) There is No Support for the Proposition That Utility May be Assessed in the Context of a "Utility Spectrum"

The Board Decision evaluated Applicants' assertions of utility within the context of a "utility spectrum", which evaluates an asserted utility within a range from "*de minimis*" to "substantial". Board Decision at pages 20 – 31. The Office Action disregards this incorrect approach and further states that "the Board's choice of language is not at issue here. The question is only whether the specification describes at least one specific and substantial utility for the claimed nucleic acid molecules." Office Action at page 31. As Applicants have repeatedly stated, it does.

The Board acknowledged that Applicants have disclosed several specific utilities for the claimed nucleic acid molecules throughout the present specification, which have been

additionally cited by the Office. *See, e.g.,* Board Decision at pages 3-4, Office Action at pages 19-20. None of these asserted utilities have been contested by the Office as being inoperable, unbelievable or incapable of being achieved using the claimed nucleic acid molecules. Rather, the Office rests its determination that the present invention lacks utility on the incorrect analysis that "the facts in this case represent the lowest end of the [utility] spectrum, i.e., an insubstantial use." Board Decision at page 23, Office Action at page 12.

The Board asserts that there is allegedly a "spectrum" in the biochemical arts for determining whether an invention satisfies the utility requirement of 35 U.S.C. § 101. According to the Board Decision, the claimed nucleic acid molecules have utility that would "represent the lowest end of the spectrum, *i.e.*, an insubstantial use." Board Decision at page 23, Office Action at page 12. This type of analysis is improper and has no support in law. The evaluation by the Board of the utility requirement in the context of an asserted "utility spectrum" misconstrues the requirements of 35 U.S.C. § 101, "devising out of whole cloth novel propositions of law". *Paulik v. Rizkalla,* 760 F.2d 1270, 1276, 226 U.S.P.Q. 224, 228-229 (Fed. Cir. 1985) (Rich, J., concurring).

It is undisputed in patent jurisprudence that "[t]he basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility." *Brenner v. Manson,* 383 U.S. 519, 534, 86 S.Ct. 1033, 1042, 148 U.S.P.Q. 689, 695 (1966). It is further well-settled law that substantial utility is shown "where specific benefit exists in currently available form". *Brenner,* 383 U.S. at 543-535. This benefit has never been evaluated in the context of a spectrum, as the Board asserts. Rather, practical utility for an invention turns on a factual analysis of the disclosure of the specification to determine simply if there is a benefit that is specific and currently available. *Cross v. Iizuka,* 753 F.2d 1040, 1044, 224 U.S.P.Q. 739, 742 (Fed. Cir. 1985). *Brenner* says that a future benefit "which either has no known use or is useful only in the sense that it may be an object of scientific

research" is not substantial, but *Brenner* does not suggest that a benefit that is known and currently available is, or could be, insubstantial. *Brenner,* 383 U.S. at 534-535.

The Board Decision asserts that "[r]ather than setting a de minimis standard, § 101 requires a utility that is 'substantial', i.e., one that provides a specific benefit in currently available form." Board Decision at page 20, Office Action at page 10 (underlining in original). While Applicants agree that the claimed invention provides a specific benefit in currently available form, the Board's suggestion that this benefit is evaluated within some asserted "spectrum" of utility institutes a new standard of utility that is not supported by the current law. To the contrary, it is well-settled that "[t]he threshold of utility is not high: An invention is 'useful' under section 101 if it is capable of providing some identifiable benefit." *Juicy Whip, Inc. v. Orange Bang, Inc.,* 185 F.3d 1364, 1366, 51 U.S.P.Q.2d 1700, 1702 (Fed. Cir. 1999), *citing Brenner v. Manson*, 383 U.S. at 534. Furthermore, an invention need only provide one identifiable benefit to satisfy 35 U.S.C. § 101. *See Raytheon Co. v. Roper Corp.*, 724 F.2d 951, 958, 220 U.S.P.Q. 592, 598 (Fed. Cir. 1983) ("when a properly claimed invention meets at least one stated objective, utility under section 101 is clearly shown").

The Board relies on *In re Kirk* and *In re Ziegler* to support its position that utility must be evaluated in some sort of spectrum and that a *de minimis* utility constitutes an "insubstantial use". *See* Board Decision at pages 16-23, Office Action at pages 6-12. However, these cases support no such requirement nor are they applicable to the present disclosure. The court in *Kirk*, for example, found that no utilities had been asserted in the specification for the claimed intermediates. Rather, the specification merely asserted that the compounds had "value as intermediates" and possessed "biological activity". *In re Kirk* 376 F.2d at 938. Furthermore, the applicants in *Kirk* did not even suggest that the claimed steroid compound intermediates had any known use. *Id.* at 941-942. In that case, the court merely found that "[i]t is what the compounds

are disclosed to do that is determinative" in the utility analysis. *In re Kirk*, 376 F.2d at 941 (emphasis added). This is far from finding that utility must be analyzed as part of a spectrum.

Nor does the decision in *In re Ziegler* support such a proposition. In fact, the facts in *Ziegler* concerning the disclosed utility of the claimed chemical compound were much like the facts in *Kirk* in that the only disclosed utility for the granules of polypropylene were that "they could be pressed into a flexible film with a characteristic infrared spectrum and that the polypropylene was 'plastic like' ". *In re Ziegler,* 992 F.2d 1197, 1203, 26 U.S.P.Q.2d. 1600, 1605 (Fed. Cir. 1993). Thus, the finding of a lack of utility in *Ziegler* is in accordance with *Kirk* in that there must be an identifiable benefit in currently available form disclosed in the specification. *In re Kirk,* 376 F.2d at 945. This is all that is required in the utility analysis.

In contrast to the cases relied upon by the Board and discussed above, the claimed nucleic acid molecules have been proven to work for a specific, *i.e.*, not vague or unknown benefit – they identify the presence or absence of a polymorphism. This benefit is immediately realized directly from the use of the claimed nucleic acids, not from the use of other molecules. Such a proven use that provides an acknowledged known benefit to the public satisfies the utility requirement of 35 U.S.C. § 101.

(3) Probes for Other Molecules or Source for Primers

In addition to the use of the claimed nucleic acid molecules to identify the presence or absence of a polymorphism, Applicants have asserted that the claimed nucleic acid molecules can be used as probes for isolating additional nucleic acid molecules in other plants and organisms and as a source of primers. Appellant's Brief filed January 31, 2001 ("Appellant's Brief"), at pages 16-18; specification at page 24, line 4 through page 28, line 2. Once again, the Office has not challenged that the claimed nucleic acid molecules could be used in this manner, but rather argues "[w]hile that may be true, it begs the question of what substantial use such knowledge would have?" Board Decision at page 24, Office Action at page 13. To this end, the Office is

again applying an improper test for utility, and fails to recognize that this utility is useful in and of itself and not simply a step toward a "more useful" result.

Applicants have provided a specific utility for the claimed nucleic acid molecules as probes for related nucleic acid molecules in other species and to isolate a promoter active in young seed pods (5 to 15 days after flowering) via a chromosome walk.[13] For example, the specification discloses that the claimed nucleic acid molecules can be used to isolate nucleic acid molecules of other plants and organisms such as alfalfa, rice, potato, cotton, oat, rye, barley, maize, wheat, *Arabidopsis*, *Brassica*, *etc.*[14] Specification at page 24, lines 13-26. Additionally, Applicants have specifically disclosed that one use of the claimed nucleic acid molecules is to initiate a chromosome walk. Specification at page 25, line 20 through page 26, line 20. The Office denigrates that utility when it asserts that the claimed nucleic acid molecules "at best...can be used to initiate a 'chromosome walk' cloning procedure" and that "[a]ny nucleic acid molecule from any plant cell generally serves this purpose...." Final Action at page 13. *See also* Advisory Action at pages 15-16. While similar utilities are shared by a class of nucleic acid molecules, these asserted utilities are specific to SEQ ID No. 1.

In short, the Office appears to be arguing that this utility is not a legal utility simply because other molecules can be used for the same purpose, *i.e.*, chromosome walks. That position is wrong as a matter of law – there is no requirement of exclusive utility in the patent

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[13] The Board Decision attempts to introduce ambiguity into this asserted utility by implying that it is not clear whether the claimed nucleic acid molecules have the ability to isolate a promoter in young seed pods (5 to 15 days after flowering) because the disclosure in the specification states that the claimed nucleic acid molecules were obtained from young seeds collected from young pods. Board Decision at page 25. One skilled in the art would know that because the claimed nucleic acid molecules were isolated from young seeds collected from young pods, they will provide an appropriate starting point for isolating a promoter that is active in young seed pods. Moreover, the specification clearly states source of the isolated nucleic acid molecules of the present invention and the Wiegand Declaration confirms this source. *See* specification at page 67, lines 10-22 (Example 1); Wiegand Decl. at ¶ 4.

[14] Furthermore, one skilled in the art of hybridization and amplification understands how to design and utilize probes and primers to target a sequence of interest, and therefore it is not necessary for Applicants to provide a laundry list of each and every nucleic acid molecule that can be identified using the claimed nucleic acid molecules.

law. *See Carl Zeiss Stiftung v. Renishaw PLC*, 945 F.2d 1173, 1180, 20 U.S.P.Q.2d 1094, 1100 (Fed. Cir. 1991) ("An invention need not be the best or the only way to accomplish a certain result..."). Such an argument would imply that a new golf club has no legal utility because other golf clubs can be used for the same purpose, *i.e.*, hitting golf balls. That position must be rejected as it requires reading "into the patent laws limitations and conditions which the legislature has not expressed," a practice condemned by the Supreme Court. *See Diamond v. Chakrabarty*, 447 U.S. 303, 308, 206 U.S.P.Q. 193, 196 (1980), *quoting United States v. Dubilier Condenser Corp.*, 289 U.S. 178, 199, 17 U.S.P.Q. 154, 162 (1933).

Moreover, it is factually incorrect that random nucleic acid molecules would provide as good a starting point for a chromosome walk as would the claimed nucleic acid molecules. The claimed nucleic acid molecules provide a particularly appropriate and demonstrably useful starting point for a walk to isolate a promoter that is active in young seed pods (5 to 15 days after flowering). It is also factually incorrect that there is no well-established use for such a promoter, as is asserted in the Advisory Action at pages 15-16. Isolation of such a promoter would be desirable and particularly useful because it allows expression of proteins at that important developmental state. Because the claimed nucleic acid molecules were isolated from young seed pods, they provide an appropriate starting point for isolating a promoter active in young seed pods. A random nucleic acid molecule does not provide an equally good starting point to isolate such a promoter. Furthermore, even if a random nucleic acid molecule provided a <u>better</u> starting point than the claimed nucleic acid molecules, it would not obviate the utility of the claimed nucleic acid molecules. An invention may be "less effective than existing devices but nevertheless meet the statutory criteria for patentability." *Custom Accessories, Inc. v. Jeffrey-Allan Indus.*, 807 F.2d 955, 960 n.12, 1 U.S.P.Q.2d 1196, 1199 n.12 (Fed. Cir. 1986).

The Board also applies this improper standard for utility when it analogizes the utility of the claimed nucleic acid molecules as probes, as a source to isolate primers, and in a

chromosome walk to that of an analgesic that has been disclosed as being useful "because it can be used to fill a jar, which would then be useful as a paperweight." Board Decision at page 26. Such an analogy is inapposite. The utility of the claimed nucleic acid molecules for detecting a polymorphism or for initiating a chromosome walk, for example, "is convincing to one of ordinary skill in the art", whereas the utility of the claimed nucleic acids as a paperweight would not be. *In re Jolles,* 628 F.2d 1322, 1326, 206 U.S.P.Q. 885, 890 (C.C.P.A. 1908). As Applicants have asserted above, such an argument would imply that a new golf club lacked utility because it was useful for hitting golf balls. Rather, a new golf club would have utility because it was designed to hit golf balls in a particular manner. Likewise, the claimed nucleic acid molecules can be used to identify a particular trait or sequence in a sample, cell or organism.

Moreover, the analogy offered by the Board comparing the presently disclosed utilities to that of a paperweight would suggest that the claimed nucleic acid molecules have been disclosed as being useful because they contain nucleotides. This is not the case. Rather, the claimed nucleic acid molecules have been asserted as being useful because they can be used to identify corresponding nucleic acid molecules.[15] Unlike the paperweight comparison, this utility is intrinsic and specific to the claimed nucleic acid molecules and not to all nucleic acid molecules in general.

Knowing that the nucleic acid molecules of the present invention can be used to isolate corresponding molecules in other plants and organisms and to identify a particular region of interest in a genome, such as a promoter sequence, is a substantial and specific utility. The fact that an isolated EST sequence can be used as a genetic probe is in itself useful as a tool to a

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[15] Applicants have submitted proof that the claimed nucleic acid molecules can be used in this very manner. *See, e.g.,* Wiegand Decl. at ¶s 12-17. The Board Decision disregards this evidence based on the assertion that it is not clear what a "true enough copy of SEQ ID No. 1" is. Board Decision at page 26. This issue has been addressed in Section 2.A.(2)(d) *supra* and ignores the statements made in ¶ 16 and Appendix A of the Wiegand Declaration. Furthermore, the Second La Rosa Declaration clarifies the evidence submitted in the Wiegand Declaration by asserting how Dr. Wiegand's experiments are understood by one of ordinary skill in the art. Second La Rosa Decl. at ¶ 7.

genetic researcher because it enables one of ordinary skill in the art to create a genetic map of a particular organism. This ability is critical to identifying and isolating regions of interest in an organism's genome.

(4) Expression Assays and Other Uses

For these reasons asserted above, Applicants' assertions that the claimed nucleic acid molecules may be used to measure the level of mRNA in a sample and introduced into plants or plant cells, as sense or antisense inhibitors, which can then be used to screen for compounds such as herbicides and other plant traits, much like a cell-based assay, also satisfy the utility requirement of § 101. *See* specification at page 64, line 19 through page 65, line 22; Appellant's Brief at pages 10-11. These asserted utilities are substantial and specific to the claimed nucleic acid molecules and no evidence has been submitted by the Board or the Office suggesting that the claimed nucleic acid molecules could not so be used.

The Office argues, essentially, that the specification does not assert that use of the claimed nucleic acid molecules as sense or antisense inhibitors is feasible and that such a use "does not provide a specific or substantial benefit in currently available form." Board Decision at page 27, Office Action at page 15. Additionally, while the Office acknowledges that the Wiegand Declaration specifies "[a] nucleic acid molecule of SEQ ID NO: 1 can also certainly be used to detect expression level", Wiegand Decl. at ¶ 14, the Board Decision finds that "the asserted utility of the claimed nucleic acid – as one component of an assay for monitoring gene expression – does not satisfy the utility requirement of § 101." Board Decision at page 28, Office Action at page 16. This interpretation of the utility requirement is simply wrong. Simply because the use of additional nucleic acid molecules would provide further information about the genome of, for example, a particular plant or organism, does not mean these asserted utilities are *de minimis*, non-specific, or do not provide an immediate benefit. As Applicants have previously stated, there is no legal support for the proposition that utility, in the sense of 35 U.S.C. § 101,

may be assessed as part of a spectrum. There is either a substantial, specific and credible asserted utility for an invention, or there is not. "To violate [35 U.S.C.] 101 the claimed device must be totally incapable of achieving a useful result." *Brooktree Corp.*, 977 F.2d at 1571.

Along this same line, the argument that "appellants claim a product asserted to be useful in a method of generating gene-expression data, but the specification does not disclose how to interpret those data" must also fail. Board Decision at page 29, Office Action at page 17. As stated above, where the utilities of a claimed invention are well-known and accepted by those of ordinary skill in the art, there is no requirement to specifically provide this information. *See In re Gaubert,* 524 F.2d at 1224; *See also Cross v. Iizuka,* 753 F.2d at 1044 ("[i]t is axiomatic that an invention cannot be considered 'useful'. . . unless substantial or practical utility for the invention has been discovered and disclosed where such utility would not be obvious."); *In re Jolles,* 628 F.2d 1322, 1326, 206 U.S.P.Q. 885, 890 (C.C.P.A. 1980) ("[p]roof of utility is sufficient if it is convincing to one of ordinary skill in the art.")

B. The Claimed Nucleic Acid Molecules Provide Practical, Real World Benefits, *i.e.*, They Have Substantial Utility

The Office has asserted that the disclosed uses are legally insufficient or "insubstantial" under 35 U.S.C. § 101, allegedly because while the claimed nucleic acid molecules are useful "to some degree", the disclosed uses allegedly do not represent a substantial utility. Board Decision at page 24, Office Action at page 13. The Office asserts that there is allegedly a "utility spectrum," but such a position has no basis in law. The touchstone of "substantial" utility is "real world" or "practical utility." *See, e.g., Fujikawa v. Wattanasin*, 93 F.3d 1559, 1563, 39 U.S.P.Q.2d 1895, 1899 (Fed. Cir. 1996). "'Practical utility' is a shorthand way of attributing 'real world' value to claimed subject matter. In other words, one skilled in the art can use a claimed discovery in a manner which provides some immediate benefit to the public." *Nelson v. Bowler*, 626 F.2d 853, 856, 857, 206 U.S.P.Q. 881, 883 (C.C.P.A. 1980) ("tests evidencing

pharmacological activity may manifest a practical utility even though they may not establish a specific therapeutic use").[16]

There can be no question that one skilled in the art can use the claimed nucleic acid molecules in a manner which provides an immediate benefit to the public. *See, e.g.*, Wiegand Decl. at ¶s 20, 23. Applicants have disclosed numerous utilities for the claimed nucleic acid molecules, and have submitted evidence proving that the claimed nucleic acid molecules work for at least two of the disclosed utilities. *See Id.* Furthermore, Applicants have proven that the claimed nucleotide sequence alone, *i.e.*, the claimed invention in "readily apparent form," is all that is necessary to use the claimed nucleic acid molecules for the disclosed utilities, *e.g.*, to detect the presence or absence of polymorphisms. *See* Wiegand Decl. at ¶s 22-23. The detection of polymorphisms provides an immediate benefit to the public because, *e.g.*, it "enables a plant breeder to determine the distribution of parental genetic material in the progeny of a cross." Wiegand Decl. at ¶ 20. Because the evidence of pharmacological activity in *Nelson* was deemed to provide an immediate benefit and thus a practical utility, the tests submitted here that evidence detection of a polymorphism must likewise be deemed to evidence practical utility.

Quite apart from the detection of polymorphisms, there is also no question that the public has recognized the benefits provided by the claimed subject matter, and has attributed "real world" value to such nucleic acid molecules. As Applicants have previously stated, the utility of ESTs is not merely an academic issue; the real world value of ESTs is self-evident from the growth of a multi-million dollar industry in the United States premised on the usefulness of ESTs. *See* Wiegand Decl. at ¶ 6. Like fermentation processes involving bacteria, ESTs and nucleic acid molecules with EST sequences are "industrial product[s] used in an industrial

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[16] *Accord Cross v. Iizuka*, 753 F.2d 1040, 1050, 224 U.S.P.Q. 739, 747-48 (Fed. Cir. 1985); *Rey-Bellet v. Engelhardt*, 493 F.2d 1380, 1383, 181 U.S.P.Q. 453, 454 (C.C.P.A. 1974).

process – a useful or technical art if there ever was one." *See, e.g., In re Bergy*, 563 F.2d 1031, 1038, 195 U.S.P.Q. 344, 350 (C.C.P.A. 1977).

The Office misapprehends the commercial value of ESTs. Nucleic acid molecules with EST sequences are bought and sold in the biotechnology industry, as are microarrays composed of nucleic acid molecules with EST sequences.[17] In addition, many biotechnology companies derive significant revenue from EST technology. Such technology is often licensed through agreements that require the transfer of either the clones from which the ESTs were obtained, or the information necessary to make nucleic acid molecules with the EST sequences. Wiegand Decl. at ¶ 6. The Office is clearly in error when failing to credit the value of the underlying sequenced clones, *i.e.*, the nucleic acid molecules. Indeed, it is wrongly asserted that the molecules themselves have no value in the multi-million dollar industry that has developed.

The Board Decision appears to argue that the growth of this industry is based on EST databases, clone sets, and/or microarrays, and while these tools may possess the requisite utility to meet § 101, an individual nucleic acid molecule may not. Specifically, the Board Decision asserts

> [a]lthough each nucleic acid in the assay contributes to the data generated by the assay overall, the contribution of a single nucleic acid – its data point – is only a tiny contribution to the overall picture. The Brenner Court held that § 101 sets more than a de minimis standard for utility. Therefore, the patentable utility if a gene expression assay, for example, does not necessarily mean that each tiny component of the assay also has patentable utility. A patentable utility divided by a thousand does not necessarily equal a thousand patentable utilities.

Board Decision at page 30, Office Action at pages 18-19. This argument is off base. The Office's position appears to be that if each component of a microarray lacks the requisite utility

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[17] *E.g.*, Gene Logic, Inc. builds its EST expression databases using Affymetrix's GeneChip® probe arrays, which it licenses from Affymetrix. GeneChip® probe arrays are composed of hundreds of nucleic acid molecules with EST sequences. *See* "Gene Logic To Use Affymetrix GeneChip Arrays to Build Gene Expression Database Product," Press Release, January 11, 1999 (http://www.genelogic.com/PR-GeneChip.htm), document AR3 in the Information Disclosure Statement filed July 6, 1999.

because each component presents a *de minimis* utility, then simply having more varieties of those components would make it patentable. This, however, is not how the patent laws work. While a microarray, for example, may possess a different utility than a single nucleic acid molecule, that does not negate the utility of the single nucleic acid molecule nor does it render its utility *de minimis*. The Office's position on a "spectrum" of utility is in contradiction to established law.

Applicants have proven that the claimed invention has utility. The market participants for EST products are primarily sophisticated corporations and highly knowledgeable scientists who are unlikely to make commercial and scientific decisions regarding the value of ESTs based on how the ESTs are advertised. Just as "[p]eople rarely, if ever, appropriate useless inventions," they rarely, if ever, pay for useless inventions. *Raytheon Co. v. Roper Corp.*, 724 F.2d 951, 960, 220 U.S.P.Q. 592, 599 (Fed. Cir. 1983). Quite simply, the commercial value of ESTs is proof of their real world value and of the benefits they provide to the public. This evidence cannot be ignored. The patent system was created to serve and foster growth and development in the industrial arts. If the industries themselves recognize and appreciate the value of an invention, it is not for the Patent Office to say that they are mistaken.

C. The Disclosed Utilities Are Credible to One of Skill in the Art

An assertion of utility must be accepted by the Examiner unless it would not be considered "credible" by a person of ordinary skill in the art. MPEP § 2107.02. Cases in which utility was found not to be credible are rare, and usually involve "hare-brained" utilities.[18] A

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[18] Examples of incredible utilities are given in MPEP § 2107.01 at page 2100-34, and include:

> an invention asserted to change the taste of food using a magnetic field (*Fregeau v. Mossinghoff*, 776 F.2d 1034, 227 U.S.P.Q. 848 (Fed. Cir. 1985)), a perpetual motion machine (*Newman v. Quigg*, 877 F.2d 1575, 11 U.S.P.Q. 1340 (Fed. Cir. 1989)), a flying machine operating on "flapping or flutter function" (*In re Houghton*, 433 F.2d 820, 167 U.S.P.Q. 687 (C.C.P.A. 1970)), a method for increasing the energy output of fossil fuels upon combustion through exposure to a magnetic field (*In re Ruskin*, 354 F.2d 395, 148 U.S.P.Q. 221 (C.C.P.A. 1966)), uncharacterized compositions for curing a wide array of cancers (*In re Citron*, 325 F.2d 248, 139 U.S.P.Q. 516 (C.C.P.A. 1963)), a method of controlling the aging process (*In re Eltgroth*, 419 F.2d 918, 164

challenge to the credibility of a utility is essentially a challenge directed to operability, and such a challenge must be supported by a clear statement of "factual reasons which would lead one skilled in the art to question the objective truth of the statement of operability." *In re Gaubert*, 524 F.2d 1222, 1225-26, 187 U.S.P.Q. 664, 666 (C.C.P.A. 1975); *see In re Brana*, 51 F.3d 1560, 1567, 34 U.S.P.Q.2d 1436, 1441 (Fed. Cir. 1995); MPEP § 2107.02 (at 2100-41).

The Office Action asserts that "[t]he credibility of the alleged utilities is not at issue". Office Action at page 32. However, the Office Action then goes on to assert that Applicants have not shown the claimed nucleic acid molecules are useful for identifying polymorphisms as that term is allegedly defined in the specification. *See* Office Action at page 33. The Office apparently seeks to disregard Applicants' evidence of this utility as submitted in the Wiegand Declaration because he reported finding a polymorphism between *Glycine max* and *Glycine soja*, but not necessarily between individuals of *Glycine max*. *See* Office Action at pages 34-35. The Office Action then makes the jump and asserts that Applicants' have not proven a "real world" context for this utility because the detection of polymorphisms shown in Dr. Wiegand's experiments "is not relevant to the issue at hand." *Id.* at pages 34 and 35. Thus, credibility is precisely the issue – Applicants have asserted and demonstrated that the claimed nucleic acid molecules are useful for detecting the presence or absence of a polymorphism and the Office continues to assert that "the specification fails to disclose a specific utility for the invention in this context." *Id.* at 34.

This assertion is wrong. The specification has disclosed that the claimed nucleic acid molecules are useful for detecting a polymorphism. *See* specification at page 28, line 3 through page 35, line 16. The Office has submitted no evidence that suggests this, or any other utility asserted in the specification, cannot be done. In contrast, Applicants have submitted multiple

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U.S.P.Q. 221 (C.C.P.A. 1970)), and a method of restoring hair growth (*In re Ferens*, 417 F.2d 1072, 163 U.S.P.Q. 609 (C.C.P.A. 1969)).

declarations in support of this asserted utility, despite the Office's failure to establish a *prima facie* case to support a utility rejection. *See* Wiegand Decl. at ¶s 20-23, Second La Rosa Decl. at ¶ 8, and Concibido Decl. at ¶s 3-4.

Furthermore, with respect to the references cited to support Applicants' assertion of the utility of the claimed nucleic acid molecules, the Office contends that because these were published after the filing date of the application, "these references cannot be used to support Applicant's [sic] arguments." Office Action at page 36. This position is incorrect. Applicants disclosed several utilities for the claimed nucleic acid molecules in the specification as originally filed. Unlike the applicant in *Wright* (cited by the Office), Applicants here are not relying on these references to establish the utility of the claimed nucleic acid molecules. *See In re Wright*, 999 F.2d 1557, 1562-1563, 27 U.S.P.Q.2d 1510, 1514, (Fed. Cir. 1993). Rather, Applicants have submitted references that confirm the asserted utilities originally disclosed in the application are well accepted utilities by those of ordinary skill in the art.

For example, the specification asserts that the claimed nucleic acid molecules have utility as molecular markers. Specification at page 35, line 17 through page 36, line 10. The Office has challenged this as a utility that is not substantial to one of ordinary skill in the art. Office Action at page 34. However, Foster-Hartnett *et al.*[19] and Liebhard *et al.*[20] affirm that the use of molecular markers is an important aspect of genome mapping and identifying significant genes. *See* Foster-Hartnett *et al.* at 635-636, Liebhard *et al.* at 511-512. Thus, Applicants are not relying on these references to support the assertion that the claimed nucleic acid molecules have utility. *See, e.g., In re Koller*, 613 F.2d 819, 824, 204 U.S.P.Q. 702, 706 (C.C.P.A. 1980) (recognizing, for example, that under certain circumstances, "later-issued patents and

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[19] Foster-Hartnett *et al.*, "Comparative genomic analysis of sequences sampled from a small region on soybean (*Glycine max*) molecular linkage group G", *Genome*, 45(4)634-645 (August 2002).

[20] Liebhard *et al.*, "Mapping quantitative physiological traits in apple (*Malus x domestica* Borkh.)", *Plant Molecular Biology*, 52(3):511-526 (June 2003).

publications may be used to show the state of the art existing on the date of the application in question.")

Applicants have explicitly identified specific and substantial utilities, not only in the specification, but repeatedly in Applicants' various responses. *See, e.g.,* Applicants' Response dated July 6, 1999, at pages 4-11 and Applicants' Response dated August 22, 2000, at pages 7-15. In addition, Applicants have provided evidence in the form of a declaration under 37 C.F.R. §1.132 that the claimed nucleic acids work for at least two of the asserted utilities: use to identify the presence or absence of a polymorphism; and use as a hybridization probe for expression profiling. *See* Wiegand Decl. at ¶s 19-20. Either proven utility alone is enough to satisfy the law. "To violate [35 U.S.C.] 101 the claimed device must be totally incapable of achieving a useful result." *Brooktree Corp. v. Advanced Micro Devices, Inc.*, 977 F.2d 1555, 1571, 24 U.S.P.Q.2d 1401, 1412 (Fed. Cir. 1992). Unless and until the Office can prove that the claimed invention is wholly inoperative, the rejection must be withdrawn.

It is not Applicants' burden to prove a negative, rather it is the Office's burden (not met here) to establish a reasonable basis for challenging the operability of the claimed nucleic acid molecules. *In re Langer*, 503 F.2d 1380, 1391, 183 U.S.P.Q. 288, 297 (C.C.P.A. 1974). The Office has not met that burden. On the other hand, Applicants have clearly demonstrated that a nucleic acid molecule having SEQ ID No. 1 was synthesized and that it hybridized to a naturally occurring nucleic acid molecule in soybean. Wiegand Decl. at ¶s 16-19. This hybridization ability is all that is necessary to practice many of the disclosed utilities, and is the feature which enables nucleic acid molecules with EST sequences to be routinely used, for example, to detect expression levels of corresponding naturally occurring soybean nucleic acids. Wiegand Decl. at ¶ 14. The fact that such molecules work (and work routinely) for that intended purpose is alone sufficient to establish that the claimed nucleic acid molecules possess requisite legal utility.

3. The Claimed Nucleic Acids Are Enabled by the Specification

The enablement of the claimed nucleic acid molecules has been challenged in two different ways by the Office Action. First, claims 1 and 2 were rejected as non-enabled because the claimed nucleic acid molecules allegedly lack utility and therefore cannot be enabled. Office Action at page 21. Second, claim 1 was rejected as non-enabled because one skilled in the art would allegedly not be able to "make the invention as directed to nucleic acid molecules comprising the EST of SEQ ID NO: 1, or its complete complement, and additional nucleotide sequences linked to the EST." Office Action at page 22 (emphasis in original). Both rejections are improper and must be reversed in light of Applicants' factual showing of use of the claimed nucleic acid molecules to identify the presence or absence of a polymorphism and as hybridization probes because it is well-established law that "the enablement requirement is met if the description enables any mode of making and using the invention." *Johns Hopkins University v. CellPro*, 152 F.3d 1342, 1361, 47 U.S.P.Q.2d 1705, 1719 (Fed. Cir. 1998) (emphasis added), *quoting Engel Indus. v. Lockformer Co.*, 946 F.2d 1528, 1533, 20 U.S.P.Q.2d 1300, 1304 (Fed. Cir. 1991).

A. The Claimed Invention Is Enabled Because It Has Utility

The first enablement rejection erroneously rejected claims 1 and 2 under 35 U.S.C. § 112, first paragraph, as not enabled by the specification, because the claimed invention allegedly lacks utility and therefore cannot be enabled. Office Action at page 21. This rejection has been overcome by the arguments stated above regarding utility, and by Applicants' submission of evidence in the form of multiple declarations under 37 C.F.R. § 1.132 – from scientists skilled in the art – which shows that a person skilled in the art can use and has used the claimed nucleic acid molecules for the disclosed utilities. *See* Wiegand Decl., Second La Rosa Decl. Unless and until the Examiner comes forth with evidence to rebut the objective truth of the utilities disclosed in the specification, this enablement rejection must be withdrawn as improper. *See In re Wright*,

999 F.2d 1557, 1561-62, 27 U.S.P.Q.2d 1510, 1513 (Fed. Cir. 1993); *Ex parte Lemak*, 210 U.S.P.Q. 306, 307 (Bd. App. 1981) ("pure conjecture" does not substantiate rejection for lack of enablement).

B. The Claimed Invention Is Enabled Because One Skilled in the Art Would Know How to Use the Nucleic Acids of Claim 1

The Office Action rejected claim 1 under 35 U.S.C. § 112, first paragraph, as not enabled by the specification because the specification allegedly "fails to teach one of skill in the art how to use the claimed nucleic acid molecules commensurate in scope with the claim, such that one of skill in the art could identify a target nucleic acid without undue experimentation." Office Action at page 22. Apparently, the Office alleges that claim 1 is not enabled because it "embraces an essentially infinite genus of nucleic acid molecules comprising SEQ ID No: 1." *Id.* This is not the proper test for enablement. Moreover, it is well established that the enablement requirement is met if the specification enables at least one mode of using the claimed invention. *Johns Hopkins University v. CellPro*, 152 F.3d 1342, 1361, 47 U.S.P.Q.2d 1705, 1719 (Fed. Cir. 1998).

The Office Action admits that those skilled in the art would know how to use nucleic acid molecules "consisting" of SEQ ID No. 1, but provides no reasons why those of skill in the art would not also know how to use nucleic acid molecules "comprising" SEQ ID No. 1. Office Action at page 22. Furthermore, the Office Action admits that "the claims do embrace nucleic acid molecules with predictable hybridization performance characteristics under certain well-controlled conditions". Office Action at page 40. However, the Office appears to be arguing that claim 1 is not enabled because "the claims are not limited to such nucleic acid molecules, nor do the claims include and functional limitations or intended use limitations restricting their utility to one involving hybridization, or any other function." *Id.*

It appears that the Office has taken the position that a comprising claim must be enabled for every imaginable embodiment. This argument is contrary to well-established law.[21] Moreover, as the Patent Office has admitted that the claims as written are enabled, they cannot now rewrite the claims to encompass hypothetical limitations and then argue that these hypothetical limitations are not taught. The claims must be examined as they are presented to the Patent Office.

(1) Enablement Does Not Require the Art Worker to Predict *a Priori* the Operative Species in a Claimed Genus

The Office apparently contends that that the test for enablement hinges on whether one skilled in the art can "predict *a priori* with a reasonable degree of certainty the identity of claimed nucleic acid molecules suitable as a probe or primer." Final Action at page 19. *See also* Advisory Action at pages 18-20.[22] The Office Action reaffirms this position. For example, Dr. Wiegand declared that one of ordinary skill in the art would recognize that the addition of certain sequences to SEQ ID No. 1 would affect its utility, for example, as a molecular marker, however one of skill in the art would also recognize that the addition of certain sequences "such as a polylinker or a bacterial plasmid sequence such as pSport sequence would almost never adversely affect the use of a molecule comprising the particular EST sequence of interest as a molecular marker." Wiegand Decl. at ¶ 13. Yet, the Office Action disregards this, claiming "this presupposes that one would know *a priori* whether any arbitrarily chosen nucleic acid sequence was or was not soybean nucleic acid or would or would not cross-hybridize with other soybean nucleic acid molecules." Office Action at page 41. That position misses the point.

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[21] Claims are not required to exclude possibly inoperative substances. *Atlas Powder Co. v. E. I. du Pont de Nemours & Co.*, 750 F.2d 1569, 1576, 224 U.S.P.Q. 409, 413 (Fed. Cir. 1984) (citing *In re Dinh-Nguyen*, 492 F.2d 856, 858-59, 181 U.S.P.Q 46, 48 (C.C.P.A. 1974)); *Ex Parte Cole*, 223 U.S.P.Q. 94, 95 (B.P.A.I. 1983).

[22] The Advisory Action rephrases the contention, asserting that one skilled in the art cannot predict "whether any arbitrarily chosen nucleic acid sequence was or was not soybean nucleic acid or would or would not cross-hybridize with soybean nucleic acid....without knowing the identity of all soybean nucleic acid sequences." Advisory Action at page 17.

To give an easy example, one may invent and claim a carburetor, and disclose it for use in a car. While any person may envision that carburetor for use in other vehicles, one of skill in the art would immediately recognize that the claimed carburetor would not be operable, for example, in an airplane, a train, or a tractor. Even more specifically, one of skill in the art might also recognize immediately that without extensive modification, the claimed carburetor would not operate in a Porsche as it might in a Ford. In fact, without extensive modification, the claimed carburetor might *only* operate in vehicles made by Ford. These restrictions, however, would not invalidate a claim directed to a carburetor "comprising" additional elements.

In much the same way, the claimed nucleic acid molecules comprise specific elements (*i.e.,* the nucleotide sequence of SEQ ID No: 1) and have been disclosed to work for certain utilities (*e.g.,* detecting a polymorphism). No more is required under the patent laws. One of ordinary skill in the art would readily recognize operative embodiments of the claimed nucleic acid molecules, or could determine operative embodiments through due experimentation. Returning once again to the example of a carburetor, where the carburetor was disclosed for use in a car, but the claims might additionally cover the same carburetor used in an airplane, a tractor, a train, or spaceship, that claim would not be invalid. Simply because numerous embodiments or combinations including the claimed carburetor may be imagined does not render the claim invalid where one of ordinary skill in the are would be able to practice the claimed invention without undue experimentation. In the same way, of ordinary skill in the art would be able to use the claimed nucleic acid molecules for the utilities disclosed throughout the specification without under experimentation. Applicants have submitted a declaration by one skilled in the art supporting this point (*see, e.g.,* Wiegand Decl. at ¶ 13) and the Office has submitted no evidence that would reasonably contradict this assertion.

The Office attempts to turn the enablement requirement on its head by asserting that "[w]hile the claims do embrace nucleic acid molecules with predictable hybridization

performance characteristics. . . the claims are not limited to such nucleic acid molecules". Office Action at page 40. From this, the Office concludes that "[t]he claims embrace many embodiments that would simply not function appropriately in hybridization. . . and the specification does not teach how to use the large number of embodiments that are inoperative for hybridization." *Id.* This position completely mischaracterizes the enablement requirement by first construing the word "comprising" to envision any possible embodiment for the claimed nucleic acid molecules out of context of the specification and then claiming that a number of these embodiments would be inoperative. This is not the correct standard to apply to the enablement analysis. *See, e.g., CFMT, Inc. v. Yieldup Intl. Corp.,* 349 F.3d 1333, 1339, 68 U.S.P.Q.2d 1940, 1944-1945 (Fed. Cir. 2003) ("[t]he inoperability standard for utility applies primarily to claims with impossible limitations.") *Citing Process Control Corp. v. HydReclaim Corp.,* 190 F.3d 1350, 1359, 52 U.S.P.Q.2d 1029, 1035 (Fed. Cir. 1999) (claims found inoperable because they require violating the principle of conservation of mass); *Newman v. Quigg,* 877 F.2d 1575, 11 U.S.P.Q.2d 1340 (Fed. Cir. 1989) (claims to a perpetual motion machine ruled inoperable).

Therefore, to the extent that the Office suggests there is a requirement for precise *a priori* predictability without recourse to any experimentation, that position is without legal support. *Cf. Atlas Powder Co. v. E. I. du Pont de Nemours & Co.*, 750 F.2d 1569, 1576, 224 U.S.P.Q. 409, 413 (Fed. Cir. 1984) ("[t]hat some experimentation is necessary does not preclude enablement"). The proper test of enablement in such a situation is whether the disclosure "adequately guide[s] the art worker to determine, without undue experimentation, which species among all those encompassed by the claimed genus possess the disclosed utility." *See In re Vaeck*, 947 F.2d 488, 496, 20 U.S.P.Q.2d 1438, 1445 (Fed. Cir. 1991).

The argument presented in Appellant's Brief regarding the example of benzpyran is relevant to this argument. *See* Appellant's Brief at pages 30-31. While the Office Action alleges

that "[n]ucleic acid molecules are not analogous to many types of product, such as benzpyrans" and that nucleic acid molecules are employed "for many different uses," the Office Action also admits that not all variations of nucleic acid molecules "are suitable for uses requiring hybridization, nor would those skilled in the art even consider doing so." Office Action at pages 42-43. This is exactly the point. Much like a chemist would be able to determine, without undue experimentation which particular benzopyrans among all those encompassed by the group of substituted 2,3-diaryl-2*H*-1-benzopyrans possess antiestrogenic activity (*See In re Vaeck*, 947 F.2d at 496, 20 U.S.P.Q.2d at 1445), one skilled in the art of hybridization would also be able to determine, without undue experimentation, which nucleic acid molecules comprising SEQ ID No: 1 are suitable for uses requiring hybridization.

The level of skill in the art, the extensive knowledge available to one of skill in the art, and the teachings of the present specification adequately guide the art worker to determine, after selection and without undue experimentation, which nucleic acid molecules encompassed by the claims possess the disclosed utilities. Performing routine and well-known steps cannot create undue experimentation even if it is laborious. *See In re Wands*, 858 F.2d at 737, 8 U.S.P.Q.2d at 1404; *In re Angstadt*, 537 F.2d 498, 504, 190 U.S.P.Q. 214, 218-19 (C.C.P.A. 1976). Furthermore, "[i]t is not a function of the claims to specifically exclude...possible inoperative substances." *Atlas Powder Co. v. E. I. du Pont de Nemours & Co.*, 750 F.2d 1569, 1576, 224 U.S.P.Q. 409, 413 (Fed. Cir. 1984) (citing *In re Dinh-Nguyen*, 492 F.2d 856, 858-59, 181 U.S.P.Q 46, 48 (C.C.P.A. 1974)). The case law does not require "each and every compound within a claim to be equally useful for each and every contemplated application." *Ex Parte Cole*, 223 U.S.P.Q. 94, 95 (B.P.A.I. 1983).

There is no legal requirement that each and every nucleic acid molecule encompassed by claim 1 be useful for each and every contemplated utility. What is required is that the art worker know how to determine, after reasonable experimentation, whether a particular nucleic acid

molecule selected from the group is useful for a particular utility. The Office has not contended, nor can it contend, that this is unachievable with the nucleic acid molecules of the present claims. Instead, an improper test has been manufactured and applied which requires (without legal authority) demonstration of *a priori* knowledge of whether a particular molecule within the claimed genus would work.

(2) An Art Worker Can Use the Claimed Nucleic Acids Without Undue Experimentation

The Office's assertion of non-enablement is wrongly predicated on the allegation that before the claimed nucleic acid molecules may be used as a hybridization probe or amplification primer, a skilled artisan would have to "make-and-test" a myriad of nucleic acid molecules comprising the core sequence of SEQ ID No. 1. Office Action at pages 41-42, Final Action at pages 19-20. This allegation is without basis because a skilled artisan would be guided by his knowledge of the art in view of the particular purpose for which the claimed nucleic acids would be used. Furthermore, even if "make-and-test" experimentation were required to optimize a particular hybridization process, such routine experimentation would not obviate enablement.

A specification must be enabling to one of skill in the art, *i.e.*, it must guide a person of skill in the art as to how to use the claimed invention without undue experimentation. *Minerals Separation v. Hyde*, 242 U.S. 261, 270-71 (1916); *In re Wright*, 999 F.2d 1557, 1561, 27 U.S.P.Q.2d 1510, 1513 (Fed. Cir. 1993). The specification is not addressed to a layperson, but rather to one skilled in the art, and the "level of skill in the art to which a specification is addressed may be quite high." *Gould v. Mossinghoff*, 229 U.S.P.Q. 1, 14 (D.D.C. 1985), *aff'd in part, vacated in part, and remanded sub nom. Gould v. Quigg*, 822 F.2d 1074, 3 U.S.P.Q. 1302 (Fed. Cir. 1987). *Accord Mowry v. Whitney*, 81 U.S. (14 Wall.) 620, 644 (1871); *Loom Co. v. Higgins*, 105 U.S. 580, 585-85 (1881); *DeGeorge v. Bernier*, 768 F.2d 1318, 1323 (Fed. Cir. 1985); *cf. Spectra-Physics, Inc. v. Coherent, Inc.*, 827 F.2d 1524, 1534, 3 U.S.P.Q.2d 1737, 1743

(Fed. Cir. 1987) (a specification "need not teach, and preferably omits, what is well known in the art"), *quoting Hybritech Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1384, 231 U.S.P.Q. 81, 94 (Fed. Cir. 1986).

In re Wands sets forth eight factors which may be considered in determining whether a claimed invention would require undue experimentation. *In re Wands*, 858 F.2d 731, 737, 8 U.S.P.Q.2d 1400, 1404 (Fed. Cir. 1988). The *Wands* factors are illustrative, and consideration of any or all of the factors is not mandatory, *i.e.*, they provide a useful analytical framework which may be used to organize and consider the whole of the evidence on enablement. *See, e.g., Enzo Biochem v. Calgene*, 188 F.3d 1362, 1371 (Fed. Cir. 1999) (not necessary to review all of *Wands* factors); *Amgen v. Chugai Pharmaceutical*, 927 F.2d 1200, 1213, 18 U.S.P.Q.2d 1016, 1027 (Fed. Cir. 1991) (the *Wands* factors are "illustrative, not mandatory"); *In re Wands*, 858 F.2d 731, 737, 8 U.S.P.Q.2d 1400, 1404 (Fed. Cir. 1988) (determination of undue experimentation is "a conclusion reached by weighing many factual considerations"). A reasonable analysis of these factors leads to the conclusion that it would not require undue experimentation to use the nucleic acid molecules of claim 1.

The first factor is the quantity of experimentation necessary. A considerable amount of experimentation is permissible if it is routine. *In re Wands*, 858 F.2d at 737, 8 U.S.P.Q.2d at 1404. While the claimed invention encompasses a class of nucleic acid molecules, it is well within the routine skills of a person of ordinary skill in the art to use many members of that class as hybridization probes or amplification primers. Furthermore, the "make-and-test" quantum of experimentation is reduced by the extensive knowledge, for example of hybridization and primer parameters, to which a person of ordinary skill in the art has access. *See, e.g.*, the hybridization parameters set forth in Sambrook *et al.* (eds.), *Molecular Cloning: A Laboratory Manual*, 2d ed., pp. 9.47-11.61, Cold Spring Harbor Laboratory Press, Plainview, New York (1989) and Haymes *et al.*, *Nucleic Acid Hybridization, A Practical Approach*, IRL Press, Washington, DC (1985).

Accordingly, the addition of nucleotides to the recited sequence that would not alter the hybridization ability of such nucleic acid molecules is well within the skill of those working in this technology.[23] *See* Wiegand Decl. at ¶ 13; Advisory Action at page 18.[24]

The second and third factors are the amount of direction or guidance presented, and the presence or absence of working examples. The specification provides guidance to those of ordinary skill in the art. One example of the guidance provided is the citation to, and incorporation by reference of, standard resource materials that describe specific conditions and procedures for the construction, manipulation, and isolation of macromolecules. Specification at page 66, line 26 through page 67, line 6. Other examples of the guidance provided are the disclosure of illustrative hybridization conditions (specification at page 17, lines 8-21), the citation of references setting forth methodology that includes the hybridization of nucleic acid molecules to detect polymorphisms (specification at page 29, line 6 through page 35, line 3), the use of primers to amplify nucleic acids in polymerase and ligase chain reactions, and in oligonucleotide ligation assays (specification at page 29, line 26 through page 31, line 24), the hybridization of nucleic acid molecules for *in situ* hybridization (specification at page 38, lines 10-22), and the hybridization of nucleic acid molecules for microarray analysis (specification at page 40, lines 14-22). The working examples in the specification, Examples 1 and 2, disclose hybridization steps and usage of primers. In particular, the working examples disclose a sequencing reaction that has a hybridization step where a universal primer hybridizes to a

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[23] Moreover, the Office admits as much when it asserts that "[a]dding nucleic acids of arbitrary length and sequence to a probe sequence, such as SEQ ID NO: 1, is *not* conventional in the art." Office Action at page 42 (emphasis in original). Yet, despite this admission that one skilled in the art would be able to predict which nucleic acids added to the claimed nucleic acid sequence would work for the uses disclosed in the specification, the Office continues to argue that Applicants have not enabled the full scope of the claims.

[24] The Advisory Action "acknowledges that a range of small nucleic acid sequences are routinely added to nucleic acids to be used as probes or primers, such as primer binding sequences for nested PCR reactions and binding sites for capture probes for amplifying hybridization signals, or linkers and adapters for cloning and vector backbones for maintenance and production of a probe." Advisory Action at page 18.

sequence present in pSport immediately 5-prime to the cDNA insert from which the disclosed sequence was obtained.

The fourth factor focuses on the nature of the invention, *i.e.*, nucleic acid molecules comprising or consisting of SEQ ID No. 1 or the complete complement of SEQ ID No. 1. The specification describes the nucleic acid sequence of SEQ ID No. 1, and the Office has admitted that this description enables nucleic acid molecules "consisting of" SEQ ID No. 1 and its complement. Final Action at pages 18-19, Office Action at pages 22-23. Moreover, the Office admits that nucleic acid molecules "comprising" SEQ ID No. 1 (the same sequence as in claim 2) which are operative as hybridization probes or primers are enabled. Advisory Action at pages 17-18, Office Action at pages 40 and 42. The nature of the invention involves using the claimed nucleic acid molecules in a variety of processes that involve a hybridization step. Practitioners in this art have available to them considerable knowledge on the conditions and approaches that can be utilized for such a step. Practitioners in this art are also prepared to try multiple methods to obtain the desired result. Wiegand Decl. at ¶s 10-11.

The fifth and sixth factors focus on the state of the art and the relative skill in the art. Methods needed to practice the invention are known in the art, as well as procedures to carry out the hybridization or primer steps. *See, e.g.*, Sambrook *et al.* (eds.), *Molecular Cloning: A Laboratory Manual*, 2d ed., Cold Spring Harbor Laboratory Press, Plainview, New York (1989); Mailga *et al.*, *Methods in Plant Molecular Biology*, Cold Spring Harbor Laboratory Press, Plainview, New York (1995); Birren *et al.*, *Genome Analysis: Analyzing DNA*, 1, Cold Spring Harbor Laboratory Press, Plainview, New York (1997); Haymes *et al.*, *Nucleic Acid Hybridization, A Practical Approach*, IRL Press, Washington, DC (1985). These references are available to guide use of the claimed nucleic acid molecules. It is clear from these resources, and particularly the guidance that they give on how to carry out hybridization and amplification steps,

that a person of ordinary skill in the art would be able to use the claimed nucleic acid molecules for the disclosed utilities.

The seventh factor considers the predictability of the art. The art to be considered here is the art associated with hybridization and amplification, and with modifying nucleic acids for use in hybridization and amplification protocols. While the "performance characteristics" of a given nucleic acid within the scope of the claimed invention may, in certain circumstances, be difficult to predict, that is not relevant to an enablement analysis.[25] Use enablement does not require *a priori* predictability. The proper enablement analysis is whether the art is sufficiently predictable such that the art worker can reliably determine "which species among all those encompassed by the claimed genus possess the disclosed utility." *See In re Vaeck*, 947 F.2d 488, 496, 20 U.S.P.Q.2d 1438, 1445 (Fed. Cir. 1991). The arts of hybridization and amplification are sufficiently predictable such that a person of ordinary skill in the art can advantageously rely upon this predictability when undertaking the disclosed utilities with the claimed nucleic acid molecules.

The eighth factor focuses on the breadth of the claims. Use enablement is satisfied when the disclosure "adequately guide[s] the art worker to determine, without undue experimentation, which species among all those encompassed by the claimed genus possess the disclosed utility." *See In re Vaeck*, 947 F.2d 488, 496, 20 U.S.P.Q.2d 1438, 1445 (Fed. Cir. 1991). Here, enablement is satisfied because the art worker is guided by the disclosure to look, for example, to known hybridization parameters in making that determination. Use of the traditional open term "comprising" in the rejected claim does not alter the fact that the claim is enabled, particularly because not every species encompassed by the claim needs to be disclosed, even in an unpredictable technology. *In re Angstadt*, 537 F.2d 498, 502-03, 190 U.S.P.Q. 214, 218 (C.C.P.A. 1976).

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[25] For a more detailed explanation of this point, see Section 3.B.(1), *supra*.

Consideration of the *Wands* factors as a whole clearly establishes that undue experimentation would not be required to practice the invention. The specification provides considerable direction and guidance and provides working examples. There was a high level of skill in the pertinent art when the application was filed, and methods to practice the claimed invention were known. The routine experimentation that is typical in the art to optimize a hybridization or amplification process is not undue experimentation. *See In re Certain Limited-Charge Cell Culture Microcarriers*, 221 U.S.P.Q. 1165, 1174 (U.S. Int'l Trade Comm'n 1983), *aff'd sub nom. Massachusetts Institute of Technology v. AB Fortia*, 774 F.2d 1104, 227 U.S.P.Q. 428 (Fed. Cir. 1985) ("the fact that experimentation may be complex...does not necessarily make it undue, if the art typically engages in such experimentation").

4. The Specification Provides An Adequate Written Description of the Claimed Invention

The adequacy of the written description has been challenged by the Office because the nucleic acid molecules of claim 1 are allegedly "not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s)...had possession of the claimed invention." Office Action at page 24. The bases for the Office's challenge are that (1) Applicants are allegedly not in possession of the genus of infinite nucleic acid molecules of claim 1, and (2) the specification allegedly does "not disclose actual reduction to practice of any nucleic acid molecules that 'comprise' SEQ ID NO: 1 other than that of a nucleic acid molecule consisting of SEQ ID NO: 1." Office Action at page 26. These are not proper bases for a written description rejection of a "comprising" claim. If they were, every "comprising" claim ever written would be invalid for failing to describe every nuance of the claimed invention.

Applicants have provided an adequate description of the claimed nucleic acid molecules that demonstrates to one skilled in the art that Applicants had possession of the claimed invention. Indeed, the Office Action agrees with Applicants that the specification provides an adequate written description of a nucleic acid molecule of claim 2, *i.e.*, nucleic acid molecules

consisting of SEQ ID No. 1 or its complement, and therefore that Applicants are in possession of those nucleic acid molecules. Office Action at page 26. Furthermore, the Office Action has also acknowledged that Applicants have possession of, and have adequately described, non-nucleotide labels, vectors, and cDNA inserts comprising SEQ ID No. 1. *Id.* at 27. The Office Action apparently failed to note that these classes of nucleic acid molecules comprising SEQ ID No. 1 are in fact nucleic acid molecules of claim 1, because these classes "comprise" SEQ ID No. 1. Therefore, the nucleic acid molecules of claim 1 are adequately described under 35 U.S.C. § 112, and the rejection must be withdrawn as improper.

A. The Specification Reflects Applicants' Possession of the Claimed Invention

The purpose of the written description requirement is to ensure that the inventors had possession of the claimed subject matter, *i.e.*, to ensure that the inventors actually invented what is claimed. *Gentry Gallery Inc. v. Berkline Corp.*, 134 F.3d 1473, 1479, 45 U.S.P.Q.2d 1498, 1503 (Fed. Cir. 1998); *Lockwood v. American Airlines*, 107 F.3d 1565, 1572, 41 U.S.P.Q.2d 1961, 1966 (Fed. Cir. 1997); *In re Alton*, 76 F.3d 1168, 1172, 37 U.S.P.Q.2d 1578, 1581 (Fed. Cir. 1996). If a person of ordinary skill in the art would, after reading the specification, understand that the inventors had possession of the claimed invention, even if not every nuance, then the written description has been met. *In re Alton*, 76 F.3d at 1175, 37 U.S.P.Q.2d at 1584. A person of ordinary skill in the art would, after reading the present specification, understand that Applicants had possession of SEQ ID No. 1, and therefore, the claimed invention.

Applicants have provided the nucleotide sequence required by the claims, *i.e.*, SEQ ID No. 1, and have thus established possession of the claimed invention. The fact that the claims at issue are intended to cover molecules that include the recited sequences joined with additional sequences does not mean that Applicants were any less in possession of the claimed nucleic acid

molecules.[26] It is well-established that use of the transitional term "comprising" leaves the claims "open for the inclusion of unspecified ingredients even in major amounts." *Ex parte Davis*, 80 U.S.P.Q. 448, 450 (B.P.A.I. 1948). *Accord PPG Indus. v. Guardian Indus.*, 156 F.3d 1351, 1354, 48 U.S.P.Q.2d 1351, 1353-54 (Fed. Cir. 1998); *Moleculon Research Corp. v. CBS*, 793 F.2d 1261, 1271, 229 U.S.P.Q. 805, 812 (Fed. Cir. 1986).

Furthermore, the present application describes more than just the nucleotide sequence required by the claims (SEQ ID No. 1), for example, it describes vectors comprising the claimed nucleic acid molecules (specification at page 47, line 14 through page 54, line 14), and not only describes, but also deposits, the clone from which SEQ ID No. 1 was sequenced, *i.e.*, the clone designated "LIB3049-003-Q1-E1-H7." Sequence Listing at page 1; Applicants' Response dated September 13, 2000, at page 1; First La Rosa Decl. at ¶ 3.[27] Furthermore, the addition of extra nucleotides or detectable labels to the nucleotide sequence of SEQ ID No. 1, for example, is readily envisioned by one of ordinary skill in the art upon reading the present specification,[28] in particular at page 16, lines 1-10 (describing sequences with labels to facilitate detection), page 21, lines 1-9 (describing fusion nucleic acid molecules), page 25, lines 1-19 (describing

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[26] If the Office is arguing that no possession is shown because the precise claim language is not used in the specification, then it goes beyond what is required by the law. It is well-settled that the description of a claimed invention need not be *in ipsis verbis*. *Gentry Gallery v. Berkline Corp.*, 134 F.3d 1473, 1479, 45 U.S.P.Q.2d 1498, 1503 (Fed. Cir. 1998); *In re Alton*, 76 F.3d 1168, 1175, 37 U.S.P.Q.2d 1578, 1583 (Fed. Cir. 1996); *Martin v. Johnson*, 454 F.2d 746, 751, 172 U.S.P.Q. 391, 395 (C.C.P.A. 1972).

[27] While the Office admits that "[t]he specification as amended on Sept. 13, 2000 (at page 18 [sic – page 1]) includes a description of a deposited DNA clone comprising SEQ ID NO: 1", the Office argues, for the first time, that "the description of this clone added to the specification is not supported by the original specification. . ." Office Action at pages 26-27. Applicants respectfully disagree and assert this contention has been overcome by the arguments presented in Section 1 *supra* and the Second La Rosa Declarations submitted herewith.

[28] The Advisory Action asserts on one hand that the "specification does not disclose what characteristics these additional sequences may or may not have that are consistent with the operability of the nucleic acid molecules as probes or primers," Advisory Action at page 19, but on the other hand acknowledges that "a range of small nucleic acid sequences are routinely added to nucleic acids to be used as probes or primers." Advisory Action at page 18. Apparently the Advisory Action is arguing that Applicants must teach "conventional and well-known genetic engineering techniques" in direct contravention of established patent jurisprudence. *E.g.*, *Ajinomoto Co. v. Archer-Daniels-Midland Co.*, 228 F.3d 1338, 1345, 56 U.S.P.Q.2d 1332, 1337 (Fed. Cir. Oct. 3, 2000).

automated nucleic acid synthesizers that can be used to build nucleic acid molecules), and page 66, line 25 through page 67, line 6 (citing references describing the construction, manipulation and isolation of nucleic acid macromolecules).

B. Applicants Have Described the Claimed Invention

The Office Action acknowledges that "a specification need not describe conventional additions to SEQ ID NO: 1 consistent with its disclosed uses in order to adequately describe those embodiments of the claimed nucleic acid molecule, or describe every nuance of the claimed nucleic acid molecules" Office Action at page 45. However, the Office asserts that "substantial species embraced by the claims" such as "full length mRNAs, cDNAs and genes that include SEQ ID NO: 1" are not adequately described under 35 U.S.C. § 112. Final Action at page 21. The Advisory Action appears to assert that each nucleic acid molecule within the genus must be "described by complete structure." Advisory Action at page 19. *See also* Office Action at page 45 ([t]he specification discloses that the invention includes, but does not describe in any meaningful way, embodiments wherein the nucleic acid molecule contains additional nucleotides linked to SEQ ID NO: 1 in soybean nucleic acid.") These assertions are totally unfounded. An adequate written description of a genus of nucleic acids may be achieved by a "recitation of structural features common to the members of the genus." *Regents of the University of California v. Eli Lilly and Co.*, 119 F.3d 1559, 1568-69, 43 U.S.P.Q.2d 1398, 1406 (Fed. Cir. 1997). The structural feature relied upon to describe the claimed genus must be capable of distinguishing members of the claimed genus from non-members.[29] *Id.*

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[29] The Office Action confuses the issue by asserting that "the specification does not provide any structural or functional characteristics for [full length mRNAs, cDNAs and genomic sequences comprising SEQ ID No. 1]" and "the instant specification provides no distinguishing structural or functional characteristics" for proteins encoded by these nucleic acid molecules. Office Action at pages 28-29. This assertion has no basis in law. The Federal Circuit has elucidated a test for written description wherein a genus of nucleic acids may be described by a structural feature that distinguishes members of the claimed genus from non-members of the claimed genus. *Regents of the University of California v. Eli Lilly and Co.*, 119 F.3d 1559, 1568-69, 43 U.S.P.Q.2d 1398, 1406 (Fed. Cir. 1997). There is no requirement to distinguish certain members of the claimed genus from other members of the claimed genus.

The claimed nucleic acid molecules are a genus of nucleic acid molecules having the common structural feature of SEQ ID No. 1 or its complement. This common structural feature is shared by every nucleic acid molecule in the claimed genus, and it distinguishes the members of the claimed genus from non-members. If a nucleic acid molecule such as an mRNA contains SEQ ID No. 1 (or its complement), then it is a member of the claimed genus. If a nucleic acid molecule does not contain SEQ ID No. 1 (or its complement), then it is not a member of the claimed genus. The presence of other nucleotides at either end of the recited sequence will not interfere with the recognition of a claimed nucleic acid molecule as such – it either contains the nucleotides of SEQ ID No. 1 (or its complement) or it does not.

One skilled in the art would clearly know if a nucleic acid molecule contains the nucleotide sequence of SEQ ID No. 1. One skilled in the art also knows what materially affects the basic and novel characteristics of a nucleic acid sequence,[30] especially in view of the detailed disclosure in the specification of the intended uses for the claimed nucleic acid sequences. Thus, claim 1 satisfies the written description requirement.

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[30] The Office Action acknowledges that "[i]t is conventional in the hybridization art to use vectors containing probe sequences or probe sequences comprising short nucleotide sequences, *e.g.*, adapters or capture probes for signal amplification," Office Action at page 29, which in essence is an acknowledgement that one skilled in the art knows what materially affects the ability of a nucleic acid to be used as a probe or primer.

Conclusion

In view of the foregoing arguments, it is respectfully submitted that the present application is in condition for immediate allowance, and notice of such is respectfully requested.

The Examiner is encouraged to contact the undersigned at the number provided should any additional information be necessary for allowance.

Respectfully submitted,

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